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Massachusetts Department of Public Health
Minutes of the Drug Formulary Commission
Meeting of Thursday, December 17, 2015
Henry I. Bowditch Public Health Council Room, 2nd Floor
250 Washington Street, Boston, MA

Date of Meeting: Thursday, December 17, 2015
Beginning Time: 2:12 PM
Ending Time: 5:20 PM

Advisory Council Members Present: The following thirteen (13) appointed members of the Drug Formulary Commission attended on December 17, 2015, establishing the required simple majority quorum (9) pursuant to Massachusetts Open Meeting Law (OML): DPH Associate Commissioner Lindsey Tucker (Chair); Dr. Douglas Brandoff; Cheryl Campbell; Raymond Campbell; Dr. Daniel Carr; Dr. Joanne Doyle-Petrongolo; Stephen Feldman; Dr. Kenneth Freedman; Cindy Steinberg; Dr. Jeffrey Supko; Dr. Theoharis Theoharides; Tammy Thomas; Dr. Alexander Walker.

1. Welcome and Introductions

Department of Public Health (DPH) Associate Commissioner and Advisory Council Chair Lindsey Tucker called the meeting to order at 2:12PM and provided brief introductory remarks.

Ms. Tucker reminded the attendees that this is a recorded, public hearing, and confirmed that no one in audience was recording.

Ms. Tucker summarized the November 5, 2015 meeting, including discussion on comments and written testimony received from stakeholders. She reminded the attendees that written testimony and minutes are available online. She noted that the Commission achieved a significant milestone by live-editing and voting to approve the monograph that will be used to evaluate individual drug products for placement on the formulary as a potential therapeutically equivalent substitute, noted the substantial discussion that occurred regarding the placement of four FDA approved ADH labelled drug products on the formulary as a potential therapeutically equivalent substitute with the Commission also deciding that these drug products should go through the same process for evaluation as the other drug products with ADH claims.
Ms. Tucker continued by noting the work achieved at the last meeting enabled the Commission to make substantial progress towards completing Component 2 of the Evaluation and Review Process.

Ms. Tucker continued the discussion by reviewing for the Commission, Component 2 and once complete moving on to Component 3. Once Component 3 is complete, the Commission will have developed a Formulary.

Ms. Tucker reminded the Commission that the formulary is guidance for prescribers and is not mandatory. It will be another tool that prescribers can use but it will not be mandatory to substitute drugs just because the formulary recommends that action.

Ms. Tucker set forth the goals of today's meeting

- To continue to work on Component 2 and evaluate four drug products according to the criteria as potential therapeutically equivalent substitutes. This work will include: a presentation of each drug product through the approved monograph with a vote to be taken after each presentation to place the drug product on the formulary as a potential therapeutically equivalent substitute.
- A presentation of three data requests requested by the Commission

2. Approval of Minutes

Ms. Tucker called for approval of the minutes from the October 15, 2015 meeting.

- Motion: Dr. Doyle-Petrongolo
- Second: Stephen Feldman
- Suggested changes
  - Page 3: Change recommended by Tammy Thomas – should read:
    - "Ms. Thomas clarified that under Chapter 258, the DOI only has authority over fully insured plans; Chapter 258 also applies to coverage offered through the Group Insurance Commission which is not subject to DOI oversight."
  - Page 2: Dr. Supko noted that his last name was misspelled.
- All in favor: Motion carried unanimously.

3. Evaluation of FDA Approved ADF labeled Drug Products

Ms. Tucker noted that at the last meeting, the Commission reviewed the criteria that should be utilized to evaluate if a drug product should be placed on the formulary as a potential therapeutically equivalent substitute and that as a way to apply criteria in the evaluation process, an initial draft monograph was introduced and was live-edited by the Commission and approved.

Ms. Tucker continued that the Department was now ready to present information to the Commission, through completed monographs, for the Commission to begin evaluating of nine drug products for potential placement on the formulary as substitutes for drug products on the list as having a heightened public health risk and this process would begin with consideration of the four FDA approved drugs products with FDA approved labeling.

Ms. Tucker also asked the Commission to bear with the Department and understand that this is our first time doing this, and we recognize that this is the Commission's first time doing this.
To help with this process the Department has prepared a number of approaches for presenting the information to you and collecting your thoughts and noted that the Department's job is to guide the Commission's discussion and assist in reaching your conclusion. Ms. Tucker encouraged the members to refer to materials they received from the staff in reaching their decisions.

Ms. Tucker then invited Mr. DaviMr. Dunn to facilitate the conversation.

Evaluation and review of FDA-Approved ADF Labeled Drug Products:

Mr. Dunn presented the overview of the meeting and the four FDA approved drugs products with ADF labeling; Targiniq ER, Oxycontin CR, Hysingla ER, Embeda. The commission was reminded that there was a consensus among the members at the November to evaluate the ADF with FDA approval using the monograph process. Mr. Dunn reminded the members that the products under consideration have already been approved via the rigorous FDA process. The commission members were made aware that the review of the FDA approved ADF products will be a test of the monograph and the evaluation process. Mr. Dunn reiterated to members that drug product to be reviewed at this a future meetings would be reviewed based on the ADF technology not as a viable substitute. This substitute process will be addressed during the cross walk phase an up-coming meetings.

1. Hysingla ER
DISCUSSION: Mr. Dunn led the discussion of ADF property and summary of Hysingla ER (hydrocodone tartrate), available strengths, FDA approval dates. Crush resistant and is effective against chewing, snorting and injection.

Ms. Tucker encouraged the members to ask questions or contribute to the evaluation based on the materials they received.

Ms. Steinberg expressed concerns with the amount of information that required review in order to prior to a vote.

Mr. Dunn pointed out that Hysingla ER includes FDA approved ADF properties, that are demonstrated in the monograph.

Ms. Steinberg noted that there exist some issues with adverse effects and asked whether the drug was still marketed and if the issues had been solved.

Mr. Dunn ensured the members that the drug was still being marketed, and noted that the issue is covered in the monograph, including references in the patient package insert about precautions,

Mr. Dunn led the discussion a review of each section of the monograph.

Commission members displayed concerns regarding side effects, concomitant use with "strong laxatives", and the safety and tolerability profile.

Dr. Walker noted that constipation is a side effect of all narcotics and should not be considered as a relevant issue while evaluating these drugs.

Dr. Brandoff noted that this drug is the only one with this particular laxative warning, so it was worth discussing.

Dr. Carr suggested process of the executive summary is what we should be following for the product review. Although comfortable with Mr. Dunn distilling the information, he hopes that the information will be laid out even more simply and briefly that the monograph does. He suggested giving each member a piece of the analysis to present to the membership as a whole.

Ms. Steinberg said it is important to hear the entire description of the drug before voting, and suggested that it would be best if Mr. Dunn would highlight the most important parts of the monograph and frame questions before asking the members to recommend drugs

Ms. Tucker referred the members to the slide showing the four areas called out in the legislation for consideration by the members. She then asked them to refer to the "Evaluation Guide" that staff provided for members' packets to help them go through the monographs section by section. She offered to assign pre-work differently for the next meeting. She also reminded the members that the formulary is not mandatory for prescribers, who have a relationship with the patient that should be sufficient to avoid issues of intolerance, etc.

Dr. Carr recommended including safety and tolerability as an additional consideration.

Mr. Dunn continued his presentation with reference to the "Evaluation Guide"

Mr. Supko inquired if pharmacokinetics – bioequivalent v. therapeutic equivalence plasma concentration for single dose is publicly available? Bioequivalence requires similar pharmacokinetic properties. Without this FDA data, there will be no way to determine bioequivalence.

Ms. Tucker noted that our vendor will be providing additional information in the crosswalk component. She also noted that if a drug is placed on the substitution list, and no drugs are found to be substitutable, the ADF drug can remain on the list for a year or more, at which time a new drug may come around and be found to be appropriate for substitution.

Mr. Dunn reminded the members that Hysingla HR should be considered on its own, and suggested that many of the issues of concern may be addressed through the patient-doctor relationship and safe prescribing practices.

The members showed additional areas for concern regarding the products indication, use in opioid naïve patients, pharmacokinetic variability, and considerations when taken with a high-fat meals.

The Commission members reviewed the ADF properties of Hysingla ER and its demonstrated reduction in "drug liking " and "drug seeking" scores in the studies reviewed that were used to acquire FDA ADF labeling.

Dr. Doyle-Petrongolo asked about cost comparisons.

Mr. Dunn stated that cost information would be presented during the crosswalk component.

Dr. Walker noted that from the information presented and reviewed there was nothing to prevent the placing of Hysingla ER on the list as a potential substitute option.

ACTION: Dr. Walker moved to allow Hysingla ER into the next phase of the evaluative process, from Component 2 to Component 3. Seconded by Dr. Theoharides. Majority voted to allow Hysingla ER to move forward as a potential substitute drug with ADF technology for consideration during Component 3 of the draft formulary.

Opposed – Dr. Doyle-Petrongolo
Abstained – Ms. Steinberg

Additional Discussion:

Dr. Feldman indicated that the pharmacokinetic data was still very critical, need to see it, need to digest it before full thorough consideration.

Ms. Tucker and Mr. Dunn asked the members if there were any other categories desired are changes to the monograph.

Dr. Supko requested pharmacokinetic studies.

Dr. Theoharides indicated the need for time to analgesic effect.

Dr. Carr requested early post marking pharmacovigilance experience.

Ms. Steinberg requested how the ADF properties compared to each other, cost information.

Dr. Feldman inquired if copies of FDA discussion at the time of approval were present.

Mr. Dunn noted the requests and indicated that he would work with UMass Medical School (the vendor) to see if the requests could be incorporated.

(Discussion >82minutes for Hysingla ER)

Break 3:45- 4:00PM

OxyContin

Ms. Campbell recused herself from the discussion of this drug product and left the room for the duration of the deliberation.

Mr. Dunn led the discussion of the ADF property of Oxycontin CR, oxycodone HCL It was noted that Oxycontin CR provides a patented physical chemical barrier method that if manipulated would result in a viscous solution effective against injecting and, snorting. Mr. Dunn continued with a section, section review on the executive summary; the members showed concern with this product regarding due to evidence that ADF technology could be circumvented. Mr. Dunn noted for members that since the product reformulation with ADF technology that misuse from non-oral routes had declined.

The members debated the ability to circumvent the ADF technology as a concern against the drugs inclusion as a substitute, and concluded that additional information would need to be reviewed in order to come to a decision.

ACTION: Consensus of members to defer a vote on this matter to a future meeting, allowing time for additional information. Ms. Campbell was out of the room for this consent.

3. Targiniq ER

Ms. Campbell returned to the meeting.

Mr. Dunn led the discussion of the ADF property of Targiniq ER, oxycodone/naloxone. It was noted that Targiniq contains and antagonist component effective against snorting and injection. Mr. Dunn noted for the members that though FDA approved Targiniq was not available in the United States at this time.

It was the consensus of the members that with all the work in front of them that they focus their collective energies on products available in the US, and that once available they would consider if Targiniq would be a potential substitute item for the crosswalk.

ACTION: Dr. Brandoff moved not to consider Targaniq or other drugs that are not marketed in the United States for inclusion as a potential substitute. Dr. Carr seconded. The members voted unanimously not to consider such drugs.

(Discussion 25 Minutes Targaniq)

4. Embeda

Mr. Dunn led the discussion of the ADF property of Embeda, morphine sulfate / naltrexone. It was noted that Embeda contains and antagonist component effective against crushing, snorting. Mr. Dunn continued with a section, section review on the executive summary.

The members showed concern with this product regarding the interaction with high fat foods resulting in a reduced rate of absorption. The members sought additional information on the study that chewing could liberate the naltrexone precipitating withdrawal. The members also directed staff to provide clarification on the study that referenced the bioavailability of "morphine and naltrexone derived from crushed morphine sulfate and naltrexone hydrochloride extended release capsules versus intact product and versus naltrexone solution: a single dose, randomized-sequence, open label, three-way cross over trial in healthy volunteers; Johnson" as listed in the monograph.

Mr. Dunn indicated that he would work to clarify the statements.

It was also requested that if available the current trends of misuse/abuse need to be highlighted in the monograph to assist with the decision making process.

Additional discussion was had in the areas of pharmacokinetics, contraindications, and the ability to open the capsule.

Tammy Thomas departed at 4:30PM

ACTION: Consensus of members to defer a vote on this matter to a future meeting, allowing time for additional information.

4. Update Data Requests 4:53 pm

Ms. Tucker began this discussion by reminding the Commission Members that at their last meeting we indicated that we would provide you with an update today on the three remaining data requests that we have received from the Commission. Ms. Tucker also noted that the Commission also reviewed other data requests and after discussion of their continuing relevance, that some requests were no longer considered relevant to the work of the Commission or that the data was not within the control of the Department to provide the Commission with sufficient data results.

Mr. Tucker then invited Jon Mundy to begin a review of data elements the Department compiled.

Mr. Mundy began the discussion reviewing data requests received by the Commission noting that today he would be presenting a review of Abuse Deterrent or near Abuse Deterrent Drug Products, a review of High Multiple Provider Episodes Utilizers, and a review of Opioid Prescriptions. Mr. Mundy continued that he would also be presenting data provided by the Department on extend release/long acting opioid analgesics that have an FDA required Risk Evaluation and Mitigation Strategy (REMS) associated with them.

After presenting information listing medications with abuse deterrent claims but not within FDA-approved labeling, Dr. Theoharides asked if these medications did not have FDA-approved labeling because they were rejected or not asked for approval yet, or were waiting approval because the drug lacked information.

Mr. Mundy responded by indicating that both were reasons for a drug not to have FDA-approved labeling and that a drug indicating it has abuse deterrent claim/properties is a claim made by the manufacturer.

Mr. Mundy continued indicating the process for obtaining FDA-approved labeling is an arduous process and may takes years due to the FDA requiring post marketing data suggesting that the drug property dose prevent drug abuse.

Continuing, Mr. Mundy presented information on Schedule II and II opioid drug products associated with individuals with a specified multiple provider episode threshold; specifically, the Commission asked for data related to individuals who received prescriptions from multiple prescribers who and had them filled at multiple pharmacies.

Dr. Carr asked how an ADF claim is expressed to the public.

Mr. Mundy clarified that the claim can be a part of the package insert, but not on the label. Approval of labeling is an arduous process that requires at least 5 years of post-marketing data.

Mr. Mundy noted that in order to respond to this request, the Bureau conducted analysis on high multiple provider episode (MPE) individuals who received prescriptions for Schedule II or Schedule III opioids from at least 5 different prescribers and had them filled at a minimum of 5 different pharmacies over a 3 month timeframe (April to June 2015.)

Members asked clarifying questions about the date, to which Mr. Mundy responded.

Members asked if the 204 individuals in this data set represented the likely "Dr. Shoppers" and if we have information as to who these people are and whether any of these individuals have overdosed.

Mr. Mundy stated that we are closer to having this information than we've ever been, but we don't have it yet.

Ms. Tucker explained the creation of the "Data Warehouse" within DPH, and how this project would assist commissions like this in educating themselves.

Mr. Mundy continued by indicating the rationale for using this specific threshold and time period was that the metric is used by the Bureau of Justice Assistance (BJA) for a grant that Massachusetts and many other states receive.

Mr. Mundy was asked to explain each column presented on the slide and did so accordingly.

Mr. Mundy concluded his presentation by presenting data related to the Risk Evaluation and Mitigation Strategy (REMS) opioid drug products indicating that this information will be beneficial to the DFC because REMS is part of multi-agency, Federal effort to address the growing problem of prescription drug abuse and misuse.

Mr. Mundy continued by explain that in order to be designated as a drug product on the REMS, the drug product has to comply with new FDA-established, safety measures to reduce the risks and improve safe use of extended release (ER)/long acting (LA) opioids while continuing to provide access to these medications. A REMS designation is another way for the Commission to determine if a drug product has a higher ability to be tamper-proof or abuse deterrent and noted that REMS drugs have a better safety profile through safety measures developed by the manufacturer and approved by the FDA.

Mr. Mundy thanked the Commission for their review and indicted to Ms. Tucker his presentation was complete.

5. Closing Remarks; Adjournment

Ms. Tucker thanked the Commission members for their participation today and reminded Commission members that the next schedule meeting is January 7th and that the meeting is scheduled for 9:00 AM to 12:00 PM. Ms. Tucker reminded all members of the importance of letting us know if they would not be able to make a meeting.

Several members asked if the January 7th meeting could be scheduled for the afternoon. They also asked if all available 2016 dates could be communicated.

Being no further business before the Commission, Ms. Tucker asked for a motion to adjourn.

- Motion: Dr. Doyle-Petrongolo
- Second: Raymond Campbell
- All in favor: unanimous

The Drug Formulary Commission meeting concluded at 5:20 PM.

Documents Presented to DFC at the *December 17, 2015* Meeting

Documents can be found at: http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/drug-formulary-commission.html